REMARKS

This Amendment is submitted in reply to the Office Action mailed on September 22, 2003. In the Office Action, the Examiner maintained that the previously asserted election requirement was proper and made the election requirement final. Consequently, the Examiner asserted that claims 6-12 are withdrawn from consideration in the present application as allegedly being directed to a non-elected invention. Also, in the Office Action, the Examiner rejected claims 1-5. With this Amendment, no claims are amended, withdrawn claims 6-12 are canceled, and new claims 13-37 are added. Upon entry of this Amendment, the above-identified application will include claims 1-5 and 13-37.

Examiner's Comment About Priority

In the Office Action, the Examiner requested that the current status of all referenced non-provisional parent applications be included in the present application. Applicant has amended the specification of the above-identified application, as indicated above, to include the current status of the parent application to the above-identified application. This amendment is believed to adequately address the Examiner's comments about including the current status of all referenced non-provisional parent applications.

Examiner's Objection to the Abstract

In the Office Action, the Examiner objected to the Abstract of the disclosure on the basis that the originally-filed Abstract was longer than 150 words. Applicant has amended the Abstract, as indicated above, such that the Abstract is now within the suggested range of 50 to 150 words. This amendment is believed to adequately address the Examiner's objection to the Abstract. Consequently, Applicant respectfully requests that the Examiner reconsider and withdraw the objection to the Abstract.

Claim Rejections Based On Obviousness-Type (Judicially-Created Doctrine) Double Patenting

In the Office Action, the Examiner rejected claims 1-5 under the non-statutory, judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-12 of U.S. Patent No. 6,297,027. In response to this rejection, Applicant is filing an executed Terminal Disclaimer under 37 CFR § 1.321(c) along with this Amendment. Applicant believes filing of this Terminal Disclaimer adequately addresses the Examiner's rejection of claims 1-5 under the judicially created doctrine of obviousness-type double patenting. Therefore, Applicant respectfully requests that the Examiner enter the Terminal Disclaimer and further requests that the Examiner reconsider and withdraw the rejection of claims 1-5 under the non-statutory, judicially created doctrine of obviousness-type double patenting based on claims 1-12 of U.S. Patent No. 6,297,027.

Claim Rejections Under the First Paragraph of 35 U.S.C. §112

In the Office Action, the Examiner rejected claims 1-5 of the above-identified application under the first paragraph of 35 U.S.C. §112 for allegedly failing to provide an adequate written description. In support of this rejection, the Examiner stated:

> Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.
>
> In so far as the instant claims are directed to allelic variants of SEQ ID NO:3, the specification lacks an adequate written description of this subject matter. The recitation of 'allelic variant' is directed to a specific molecule for which the instant specification fails to describe the molecule in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The structure of an 'allelic variant' cannot be predicated on the basis of the nucleotide sequence of SEQ ID NO:3 since there is no disclosure of where the variation occurs in the sequence of SEQ ID NO:3. The claims are

directed to a species of nucleic acid, the structure of which cannot be determined or predicted from the disclosed nucleic acid sequence and the specification does not evidence isolation or conception of the structure of an 'allelic variant', therefore the specification does not provide an adequate written description of the claimed subject matter, and thus the claimed invention, to the extent that it reads upon an 'allelic variant' was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that, 'applicant must convey with reasonable clarity to those skilled in the art that as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the written description inquiry, whatever is now claimed.' (See Vas-Cath at page 1116.)

With the exception of very particular nucleic acid sequence which is disclosed in the instant application, the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acid molecules and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The specific molecular structure is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes vs Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115). The instant claims are directed to a structure, which could be isolated, but for which, there is no written description. As in Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class because the specification provided only

> the bovine sequence. In the instant situation, the specification only provides a single nucleic acid sequence, but fails to provide a description of the "broad class" of allelic variants, regardless of whether they could be made or isolated.

The above-identified application is a continuation-in-part application based on, and claiming the priority of, U.S. patent application no. 08/688,908, which is also referred to herein as "parent application no. 08/688,908." The Examiner made no distinction between the specification of the above-identified application and the specification of parent application no. 08/688,908 when stating the present written description rejection. Nonetheless, and despite the Examiner's above-recited comments, the written description of the invention contained in parent application no. 08/688,908 is adequate to support the recited "allelic variant" terminology, as defined in claims 1-5. The written description contained in parent application no. 08/688,908 reasonably conveys to one skilled in the relevant art that the inventor, at the time parent application no. 08/688,908 was filed, had possession of the invention, as defined in claims 1-5 of the above-identified application.

In subsequent comments, references to parent application no. 08/688,908 are sometimes made with respect to U.S. Patent No. 6,297,027, which issued from parent application no.08/688,908. A copy of U.S. Patent No. 6,297,027 is attached as Exhibit A; U.S. Patent No. 6,297,027 is also referred to herein as the "Spurlock patent."

The written description requirement of the first paragraph of §112 reads as follows:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The test for compliance with the written description requirement is well settled:

> The purpose of the 'written description requirement is broader than to merely explain how to 'make and use'; the applicant must also convey with reasonable clarity to those skilled in the art, that,... he or she was in possession of the invention...at the time the application was filed.

Vas-Cath, 935 F.2d at 1563-1564. Additional guidance about compliance with the written description requirement is provided below:

> One shows that one is 'in possession' of the invention by describing the invention, with all its claimed limitations, not that which makes it obvious. Lockwood, 107 F. 3d at 1565, 1572. The inventor can demonstrate possession by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention.

Vas-Cath, 935 F.2d at 1563-1564. Determination of whether the written description requirement is satisfied is a question of fact:

> The issue of whether a patent specification adequately describes the subject matter claimed is a question of fact.

Vas-Cath, 935 F.2d 1555, 1563. Therefore, a fact-based analysis of the specification of the present application is needed to evaluate the sufficiency of the written description and determine if the specification, via words, examples, structures, etc., reasonably conveys to one of ordinary skill in the art the inventor's possession of the claimed invention at the time parent application no. 08/688,908 was filed.

First, Applicant notes the following statement of the Examiner in the present Office Action:

> [T]he recitation of "allelic variant" is directed to a specific molecule for which the instant specification fails to describe the molecule in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time application was filed, had possession of the claimed invention.

is erroneous. Rather than merely relating the term "allelic variant" to a single specific molecule, the disclosure of parent application no. 08/688,908 variously and fully characterizes allelic variants using words, structures, and examples. The disclosure of parent application no. 08/688,908 demonstrates the inventor had possession of a DNA sequence encoding a bovine leptin polypeptide and also had possession of allelic variants of the DNA sequence encoding the bovine leptin polypeptide at the time parent application no. 08/688,908 was filed.

Various descriptive means, such as words, examples, and structures, employed in parent application no. 08/688,908 demonstrate to a person of ordinary skill in the art that Applicant had possession of allelic variants of the bovine leptin DNA at the time parent application no. 08/688,908 was filed. For example, parent application no. 08/688,908 discloses a DNA sequence of the bovine leptin polypeptide that is identified as SEQ ID NO:3. (See column 5, lines 46-51, and Figures 1, 2A, and 2B of U.S. Patent No. 6,297,027 of Exhibit A). Next, parent application no. 08/688,908 uses words to describe an allelic variant of the bovine leptin DNA by stating the allelic variant or 'variant' is a DNA molecule that is substantially similar to the bovine leptin DNA sequence identified as SEQ ID NO:3. (See column 5, lines 17-19 of U.S. Patent No. 6,297,027 of Exhibit A). Parent application no. 08/688,908 further discloses that allelic variants of the bovine leptin DNA sequence may have any combination of deletions from, insertions in, or substitutions to SEQ ID NO:3, as long as the desired leptin activity is observed. (See column 5, lines 25-34, of U.S. Patent No. 6,297,027 of Exhibit A). Furthermore, parent application no. 08/688,908 discloses that allelic variants may exist as mutations of the bovine leptin DNA identified as SEQ ID NO:3. (See column 5, lines 23-25, of U.S. Patent No. 6,297,027 of Exhibit A).

The factual evidence presented above demonstrates that parent application no. 08/688,908 describes allelic variants of the bovine leptin DNA in terms of variations of the DNA sequence identified as SEQ ID NO:3, where the variations may include any combination of deletions, insertions or substitutions to the DNA sequence identified as SEQ ID NO:3, with the caveat that the variations are substantially similar to the DNA sequence identified as SEQ ID NO:3. This composite description of the allelic variants of the bovine leptin DNA is believed to reasonably provide an adequate written description of allelic variants of the bovine leptin DNA sequence, as defined in claims 1-5 of the above-identified application. Additionally, this composite description of the allelic variants of the bovine leptin DNA in parent application no. 08/688,908 demonstrates that parent application no. 08/688,908 reasonably conveys to a person of ordinary skill in the art that Applicant had possession of allelic variants of the bovine leptin DNA when parent application no. 08/688,908 was filed. Consequently, the disclosure in parent application no. 08/688,908 is adequate to fulfill

the written description requirement of the first paragraph of §112 with the respect to allelic variants, as defined in claims 1-5 of the above-identified application.

Next, Applicant notes the words used to describe "allelic variant" in parent application no. 08/688,908 are consistent with the words used by a person of ordinary skill in the art to describe "allelic variant." For example, the word "allele," which is the linguistic basis for the term "allelic," is defined as follows:

> "any one or more of alternative forms of a given gene. They [allele] occur by mutation, where deletions, substitutions or insertions have altered the original specific sequence of nucleotides."

See page 13 of Language of Biotechnology, A Dictionary of Terms (attached as Exhibit B of this Amendment). The term "variant" is defined as "a strain which differs from other related strains in a specified or specified way." See page 819 of the Dictionary of Genetics (6th Edition) (attached as Exhibit C of this Amendment). Thus, the description of allelic variants of the bovine leptin DNA in parent application no. 08/688,908 in terms of variations of the DNA sequence identified as SEQ ID NO:3, where the variations may include any combination of deletions, insertions or substitutions to the DNA sequence identified as SEQ ID NO:3, with the caveat that the variations are substantially similar to the DNA sequence identified as SEQ ID NO:3, is entirely consistent with the "allele" linguistic basis for the term "allelic" and with the "variant" term, as defined in Exhibits B and C, respectively.

As noted, parent application no. 08/688,908 discloses a specific sequence of nucleotides that encode the 08/688,908 leptin polypeptide identified as SEQ ID NO:3. In addition, parent application no. 08/688,908 specifies allelic variants of the bovine leptin DNA in terms of variations of the DNA sequence identified as SEQ ID NO:3, where the variations may include any combination of deletions, insertions or substitutions to the DNA sequence identified as SEQ ID NO:3, with the caveat that the variations are substantially similar to the DNA sequence identified as SEQ ID NO:3. Thus, parent application no. 08/688,908 describes allelic variants of the bovine leptin DNA using terminology that is consistent with terminology used by one of ordinary skill in the art. Consequently, a person of ordinary skill in the art would know the inventor had possession

of allelic variants of bovine leptin DNA at the time parent application no. 08/688,908 was filed by simply reading the disclosure of parent application no. 08/688,908.

In addition, during prosecution of parent application no. 08/688,908, now U.S. Patent No. 6,297,027, Applicant submitted a Declaration under 37 C.F.R §1.131 that established the invention claimed in parent application no. 08/688,908 was made at least as early as December 26, 1995. This Declaration under 37 C.F.R §1.131 from parent application no. 08/688,908 is attached as Exhibit D of this Amendment. This Declaration under 37 C.F.R §1.131 described a DNA sequence of a 450 base clone for the bovine leptin polypeptide that was submitted by Applicant to National Bioscience, Inc.(a commercial laboratory skilled in the protocol of performing gene sequencing), for sequencing. This Declaration under 37 C.F.R §1.131 further states that National Bioscience, Inc. reported their sequence determination back to Applicant upon completion of the requested sequencing work. The DNA sequence information reported for the 450 base clone submission established that the 450 base clone for the bovine leptin polypeptide was an allelic variant of the DNA sequence of SEQ ID NO:3. Therefore, based on the disclosure of the DNA sequence of the 450 base clone for the bovine leptin polypeptide in the Declaration under 37 C.F.R §1.131 during prosecution of parent application no. 08/688,908, it is clear the inventor of the present invention, as defined in claims 1-5, had possession of other allelic variants of the bovine leptin polypeptide, beyond those explicitly disclosed in parent application no. 08/688,908, that fall within the scope of the invention described in parent application no. 08/688,908. Thus, the Declaration under 37 C.F.R §1.131 and the DNA sequence information provided therein further documents and illustrates the inventor's possession of allelic variants of bovine DNA leptin at the time parent application no. 08/688,908 was filed.

The disclosure of parent application no. 08/688,908 (see column 5, lines 5-45, of U.S. Patent No. 6,297,027 of Exhibit A) states that allelic variants of SEQ ID NO:3 are within the scope of the present invention since parent application no. 08/688,908 discloses that allelic variants of SEQ ID NO:3 could produce altered expressions of the leptin gene when different levels of fat deposition are observed in cattle. See column 1, lines 52-59 ; column 3, lines 4-17; column 3, line 13, through column 4, line 21; column 9, line 30, to column 10, line 10; and column 10, lines 23-36, of U.S.

Patent No. 6,297,027 of Exhibit A. The inventor demonstrated possession of additional allelic variants of the bovine leptin DNA reported as SEQ ID NO:3 by disclosing the identification of multiple clones containing bovine leptin DNA on different occasions. See column 6, lines 26-68; and column 12, lines 1-50 of U.S. Patent No. 6,297,027 of Exhibit A. Identification of still other allelic variants that fall within the scope of allelic variants of SEQ ID NO:3 may occur using Restriction Fragment Length Polymorphism (RFLP) techniques (see column 6, lines 7-20, of U.S. Patent No. 6,297,027 of Exhibit A) or hybridization techniques (see column 6, lines 37-63, and Example II of U.S. Patent No. 6,297,027 of Exhibit A).

Next, we consider the Examiner's allegation that the detailed description of the above-identified application is not adequate because "the structure of an 'allelic variant' cannot be predicted on the basis of the nucleotide sequence of SEQ ID NO:3. since there is no disclosure of where the variation occurs in the sequence of SEQ ID NO:3." This statement of the Examiner is an erroneous statement of the law pertaining to the written description requirement of the first paragraph of §112. As noted above, the test for meeting the written description requirement is whether a person skilled in the art is reasonably able to recognize the inventor possessed what is being claimed at the time of filing. The test for meeting the written description requirement is <u>not</u>, despite the Examiner's allegation, whether a person skilled in the art is reasonably able to recognize where a variation occurs in the sequence of SEQ ID NO:3.

Furthermore, the structure of other allelic variants within the scope of the disclosure in parent application no. 08/688,908 that are not specifically identified as SEQ ID NO:3 may be predicted on the basis of the nucleotide sequence of SEQ ID NO:3 reported in parent application no. 08/688,908. As disclosed in parent application no. 08/688,908, the disclosed genetic sequences and oligonucleotides allow for identification of other allelic variants of bovine leptin DNA that are well within the scope of the invention of parent application no. 08/688,908. See column 6, lines 7-11, of U.S. Patent No. 6,297,027 of Exhibit A. Parent application no. 08/688,908 further discloses that identification of such allelic variants of the bovine leptin DNA may occur using RFLP techniques (see column 3, lines 7-17, of U.S. Patent No. 6,297,027 of Exhibit A) or may occur using a portion or the entire DNA sequence of SEQ ID NO:3 as a probe that hybridizes to a sample containing

bovine leptin DNA (see column 6, lines 27-64, and Example II of U.S. Patent No. 6,297,027 of Exhibit A) followed by DNA sequencing or RFLP analysis. DNA sequencing or RFLP analysis are common routine techniques known to, and capable of being practiced by, persons of ordinary skill in the art without undue experimentation. Therefore, identification of other allelic variants may clearly be predicted by a person of ordinary skill in the art on the basis of the nucleotide sequence of SEQ ID NO:3 that is disclosed in parent application no. 08/688,908.

We next consider U.S. Patent Application Publication No. US 2003/0219819 A1 entitled "Method for Improving Efficiencies in Livestock Production", hereinafter referred to as the "Foley publication" (attached as Exhibit E of this Amendment). The Foley publication explicitly recognizes that U.S. Patent No. 6,297,027 discloses the bovine leptin gene, polypeptides, and allelic variants of the bovine leptin gene (see ¶ [0009] of the Foley Publication). Furthermore, the Foley publication demonstrates that if one skilled in the art follows the techniques and protocols disclosed in parent application no. 08/688,908, the person skilled in the art would have no difficulty in identifying other allelic variants within the scope of the invention of in parent application no. 08/688,908, beyond those identified as SEQ ID NO:3. Indeed, the Foley publication confirms the ability of one skilled in the art who follows the techniques and protocols disclosed in parent application no. 08/688,908 to identify other allelic variants (beyond those identified as SEQ ID NO:3) that fall within the scope of the invention of parent application no. 08/688,908.

The Foley publication states:

> ob-Gene Genotype Determination: Means of selective amplification of bovine gene are in U.S. Pat. No. 6,297,027 to Spurlock. It is possible to distinguish ob genotypes by cloning and sequencing DNA fragments from individual animals, or by other methods known in the art. For example, it is possible to distinguish ob genotypes by employing synthetic oligonucleotide primed amplification of ob gene fragments followed by restriction endonuclease digestion of the amplified product using a restriction enzyme that cuts such product from different ob alleles into discrete product fragments of differing length. Such discrete product fragments could then be distinguished using electrophoresis in agarose or acrylaminde, for example. The ob alleles identified by Buchanan et al. (2002) were distinguished by such means using a mismatch PCR-RFLP strategy wherein, the C-

> containing allele (as above) yields DNA fragments of 75 and 19 bp following digestion of the amplimer with Kpn 2I, and the T-containing allele (as above) is not cut.

¶ [0009] of the Foley Publication. Therefore, the Foley publication states that U.S. Pat. No. 6,297,027 to Spurlock makes it possible to distinguish between ob genotypes or ob alleles other than those identified by SEQ ID NO:3 by simply reading U.S. Pat. No. 6,297,027 to Spurlock. Next, the techniques and protocol used in the Foley publication are disclosed in U.S. Pat. No. 6,297,027 at column 6, lines 33-48; column 6, lines 59-67, and Example II to identify other ob alleles within the scope of the invention of U.S. Pat. No. 6,297,027 that are not identified by SEQ ID NO:3 . Furthermore, the Foley publication publicly demonstrates that a person of ordinary skill in the art could both predict and identify other allelic variants within the scope of the invention of U.S. Pat. No. 6,297,027 by simply using the information provided in U.S. Pat. No. 6,297,027. Consequently, the Foley publication, on its face, demonstrates that a person of ordinary skill in the art would understand U.S. Pat. No. 6,297,027 discloses allelic variants of the bovine leptin DNA disclosed in parent application no. 08/688,908. It is also noted that the disclosure of the Foley publication directly contradicts the Examiner's allegations that the structure of an "allelic variant" cannot be predicted based on the written description provided in parent application no. 08/688,908.

The Examiner's statement about the written description for the term "allelic variants" allegedly being inadequate "since there is no disclosure of where the variation occurs in the sequence of SEQ ID NO:3" is also improper, since an adequate written description does not require disclosure of where the variation occurs in the sequence of SEQ ID NO:3. In this regard, Vas-Cath states:

> Furthermore, the written description requirement does not require identical descriptions of claimed compounds, but it requires enough disclosure in the patent to show one of ordinary skill in the art that the inventor 'invented' what is claimed. Vas-Cath, 935 F.2d at 1563.
>
> 'Although the exact terms need not be used in *haec verba*, see Eiselstein v. Frank 52 F. 3d 1035, 1038, 34 U.S.P.Q. 2D (BNA) 1467, 1470 (Fed Cir. 1995) ('The prior application need not describe the claimed subject matter in exactly the same terms as used in the claims ....'), the specification must contain an equivalent description of the claimed subject matter.' Lockwood, 107F. 3d at 1572.

> 'The invention claimed in the later application does not have to be described in the prior application in *ipsis verbis* in order to satisfy the description requirement of section 112. . . .and one skilled in the art, following the teaching of the prior application must be able to produce the subject matter of the later claims.' Ralston, 772 F. 2d at 1570.

Therefore, as stated in Vas-Cath, the written description does not require an identical description of the claimed allelic variant, despite the Examiner's contention to the contrary. Instead, the written description may contain "an equivalent disclosure." Parent application no. 08/688,908 does contain such"an equivalent disclosure," as documented by the various discussions provided above, such as the discussion about the Foley publication. Therefore, the disclosure of parent application no. 08/688,908 supplies an adequate written description for the invention defined in claims 1-5 of the above-identified application.

Furthermore, as detailed in Ralston, if one skilled in the art can follow the teaching of an application to produce the subject matter of the claims, the written description requirement is met. The Foley publication demonstrates that one skilled in the art following the disclosure of parent application no. 08/688,908 is able to produce and identify allelic variants of SEQ ID NO:3 that fall within the scope of claims 1-5 of the above-identified application. Therefore, for this additional reason, the disclosure of parent application no. 08/688,908 meets the written description requirement with respect to claims 1-5 of the above-identified application.

Next, Applicant notes the Examiner's statement: "The claims are directed to a species of nucleic acid, the structure of which cannot be determined or predicted from the disclosed nucleic acid sequence . . . ." is erroneous. This statement of the Examiner is erroneous since the structure of various allelic variants of bovine leptin DNA were determined and predicted by others, as described in the Foley publication, using the disclosure of parent application no. 08/688,908. Furthermore, Applicant notes the Examiner's allegation "and the specification does not evidence isolation or conception of the structure of an 'allelic variant'" is improper and is not pertinent to the adequacy of the written description with regard to claims 1-5 of the present application. Instead, the test for an adequate written description is whether the specification conveys to a person of ordinary

skill in the art that the inventor had possession of invention at the time the application was filed and is not whether the specification describes the structure of a particular allelic variant.

Applicant has demonstrated possession of allelic variants that fall within the scope of the present invention by (1) providing a specific structure of the bovine leptin DNA (SEQ ID NO:3), (2) describing an allelic variant of bovine leptin DNA in terms that are used by a person of ordinary skill in the art to describe allelic variants, (3) providing specific examples of isolating allelic variants of bovine leptin DNA from a variety of sources, and (4) highlighting the Foley publication that demonstrates how a skilled artisan followed the teaching of parent application no. 08/688,908. to identify additional allelic variants that are within the scope of the present invention, as defined in claims 1-5. Therefore, Applicant has conveyed with reasonable clarity to those skilled in the art that, as of the filing date of parent application no. 08/688,908, Applicant was in possession of the present invention, as defined in claims 1-5 of the above-identified application. (See Vas-Cath at page 1116).

Applicant also respectfully disagrees with the Examiner's interpretation of Fiers v Revel and with the Examiner's allegation that "the specific molecular structure is required" to meet the written description requirement. The Examiner's statement and interpretation of Fiers is incorrect because Fiers is concerned with determining priority based on conception of an invention. As stated above, the test for compliance with the written description requirement is not concerned with conception of the structure of particular allelic variants by the inventor(s). Rather with regard to the invention defined in claims 1-5 of the present application, the test for written description compliance is whether the specification disclosure conveys to one of ordinary skill in the art that the inventor was in possession of the invention defined in claims 1-5 when parent application no. 08/688,908 was filed. Indeed, as explained at length above, Applicant has demonstrated possession of "allelic variants", as defined in claims 1-5 of the above-identified application, by described the concept of the claimed allelic variants in terms that are adequate to allow one ordinary skill in the art to recognize that the inventor(s) had possession of "allelic variants", as defined in claims 1-5 of the above-identified application, when parent application no. 08/688,908 was filed. As demonstrated by the discussion with respect to the Foley publication, parent application no.08/688,908 reasonably conveys to one of ordinary skill in the art that the inventor had possession of allelic variants of

bovine leptin DNA represented by SEQ ID NO:3 that are well within the scope of the present invention. Fiers, 984 F. 2d 1170.

The Examiner alleges that "one cannot describe what one has not conceived. See Fiddes v. Baird . . . ." However, the Examiner's interpretation and application of Fiddes v. Baird to the facts of the Examiner's written description rejection of claims 1-5 of the present application are improper. Fiddes v. Baird involved an interference pertaining to inventions claiming mammalian fibroblast growth factor. Baird's claimed invention was directed to mammalian FGF using a disclosure that set forth the amino acid sequence for bovine pituitary FGF and a theoretical DNA sequence that allegedly would encode bovine pituitary FGF. The Baird patent did not disclose any naturally-occurring gene encoding bovine pituitary FGF, any other amino acid sequence for any other mammalian FGF, or any naturally occurring gene encoding any other mammalian FGF. Consequently, in Fiddes v. Baird, the Board of Patent Appeals and Interferences decided Baird was not in possession of the naturally occurring gene for bovine pituitary FGF or any other gene for any mammalian FGF at the time the Baird application was filed.

Fiddes v Baird contrasts with the facts of the present rejection of claims 1-5 in several important ways. For example, in contrast to the Baird application, parent application no. 08/688,908 contains an adequate written description of DNA sequences (bovine leptin gene) encoding the bovine leptin polypeptide (SEQ ID NO:3), as defined via the allelic variant terminology employed in claims 1-5 of the above-identified application. Claims 1-5 define, in part, allelic variants of bovine leptin DNA that fall within the scope of the disclosure of parent application no. 08/688,908; contrasting with the Baird application, claims 1-5 do not define allelic variants of DNA sequences encoding leptin outside of the bovine genus.

Furthermore, Applicant, via the Foley publication, has demonstrated that parent application no. 08/688,908 allows a person skilled in the art to produce and identify allelic variants of the bovine leptin DNA represented by SEQ ID NO:3 that fall within the scope of the disclosure of parent application no. 08/688,908 and within the scope of claims 1-5 of the present application. Indeed, using the techniques and protocols set forth in parent application no. 08/688,908, the Foley publication structurally identified allelic variants of the bovine leptin DNA represented by SEQ ID

NO:3 that fall within the disclosure of parent application no. 08/688,908 and within the scope of claims 1-5 of the present application. In addition, no evidence of any undue experimentation using the techniques disclosed in parent application no. 08/688,908 during identification of the allelic variants of bovine leptin was reported in the Foley publication.

The foregoing comments demonstrate that Applicant was in possession of allelic variants of the bovine leptin DNA represented by SEQ ID NO:3 at the time parent application no. 08/688,908 was filed. Therefore, it is evident an adequate written description of the allelic variant terminology employed in claims 1-5 of the above-identified application existed in parent application no. 08/688,908 at the time parent application no. 08/688,908 was filed. Consequently, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-5 under the written description requirement of the first paragraph of 35 U.S.C. §112, and that claims 1-5 be allowed.

Claim Rejection under 35 U.S.C. §102(a)

In the Office Action, the Examiner rejected claim 5 under 35 §U.S.C. 102(a) as allegedly being anticipated by Genbank ACC. No. U43943, Bos taurus OBESE mRNA submission dated January 27, 1996 (hereinafter referred to as the "Tellam submission"). According to the Examiner:

> TELLAM et al. disclose a nucleic acid molecule (mRNA) which is an allelic variant of SEQ ID NO:3 of the instant application. The nucleotide sequence differs from that of SEQ ID NO:3 in length (the prior art is longer) and differs in sequence at 14 positions. This translates into 2 amino acid differences (see bolded amino acids in attached reference) and 18 additional amino acids at the N-terminus of the protein, which could be leader sequence. Therefore, the instant claim is anticipated by the prior art.

Despite the Examiner's comments, the Tellam submission does not anticipate the invention of the above-identified application, as defined in claim 5.

During prosecution of parent application no. 08/688,908, now U.S. Pat. No. 6,297,027, Applicant submitted a Declaration under 37 C.F.R §1.131 that established the invention

of parent application no. 08/688,908, as defined in the claims of parent application no. 08/688,908, was completed prior to December 27, 1995, which is the effective date of the Tellam submission. (See Exhibit D of this Amendment). Applicant has again submitted a Declaration under 37 C.F.R §1.131, which is attached as Exhibit F of this Amendment. This Declaration under 37 C.F.R §1.131 of Exhibit F by Dr. Michael E. Spurlock, the inventor of the invention of the present application, contains facts that establish the invention of parent application no. 08/688,908, as defined in the claims of parent application no. 08/688,908, was completed prior to December 27, 1995, which is the effective date of the Tellam submission.

Because the present invention, as defined in claim 5, was completed prior to the effective date of the Tellam submission, the Tellam submission does not anticipate the invention of the above-identified application, as defined in claim 5. In view of the attached Declaration of prior invention in the United States pursuant to 37 CFR §1.131 of Exhibit F that accompanies this Amendment, it is respectfully requested that the Examiner reconsider and withdraw the rejection of claim 5 under 35 U.S.C. §102(a) and that claim 5 be allowed.

Claim Rejection under 35 U.S.C. §103(a)

In the Office Action, the Examiner rejected claims 1-4 under 35 U.S.C. 103(a) as allegedly being unpatentable over the Genbank ACC. No. U43943, Bos taurus OBESE mRNA submission dated January 27, 1996 (the "Tellam submission"). According to the Examiner:

> TELLAM et al. disclose a nucleic acid molecule (mRNA) which is an allelic variant of SEQ ID NO:3 of the instant application. TELLAM et al. do not disclose single or double stranded DNA, an expression vector or plasmid comprising the DNA or a host cell transformed or transfected with the plasmid. However, at the time of the instant invention, it would have been prima facie obvious to one of ordinary skill in the art to use the mRNA molecule of TELLAM et al. to generate a DNA molecule, which could then be placed into an expression vector or plasmid, and then placed into a host cell for the purpose of propagating the nucleic acid, as well as for expression of the encoded protein of the nucleic acid of TELLAM et al. One would be motivated to do this because TELLAM et al. identify the nucleic acid as encoding bovine obesity protein (a.k.a. leptin) and this protein

> is known to be valuable in regulation of weight in animals. At the time of the instant invention, such methods and techniques were old and well known in the art, as evidence by the disclosure of the instant specification at pages 9-10, therefore, a reasonable expectation of success was also present.

Despite the Examiner's comments, the Tellam submission does not teach, suggest, disclose, or render obvious the invention of the above-identified application, as defined in claims 1-4.

During prosecution of parent application no. 08/688,908, now U.S. Pat. No. 6,297,027, Applicant submitted the Declaration under 37 C.F.R §1.131 of Exhibit D that established the invention of parent application no. 08/688,908, as defined in the claims of parent application no. 08/688,908, was completed prior to December 27, 1995, which is the effective date of the Tellam submission. Applicant has again submitted a Declaration under 37 C.F.R §1.131, which is attached as Exhibit F of this Amendment. This Declaration under 37 C.F.R §1.131 of Exhibit F by Dr. Michael E. Spurlock, the inventor of the invention of the present application, contains facts that establish the invention of parent application no. 08/688,908, as defined in the claims of parent application no. 08/688,908, was completed prior to December 27, 1995, which is the effective date of the Tellam submission.

Because the present invention, as defined in claims 1-4, was completed prior to the effective date of the Tellam submission, the Tellam submission does not teach, suggest, disclose, or render obvious the invention of the above-identified application, as defined in claims 1-4. In view of the attached Declaration of prior invention in the United States pursuant to 37 CFR §1.131 of Exhibit F that accompanies this Amendment, claims 1-4 are each allowable. Claims 2-4 are allowable for an additional reason. Specifically, claims 2-4 each depend from allowable claim 1. Consequently, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-4 and that claims 1-4 be allowed.

New Claims Added By Applicant

Applicant has added new claims 13-37. Support for new claims 13-37 is believed to exist throughout U.S. Patent No. 6,297,027 of Exhibit A, such as at column 5, lines 5-45. New claims 13-37 do not add any new matter to the above-identified application. Applicant respectfully requests consideration and allowance of new claims 13-37.

CONCLUSION

Claims 1-5 and 13-37 are believed allowable. Consequently, reconsideration and allowance of claims 1-5 is respectfully requested. Furthermore, consideration and allowance of new claims 13-37 is respectfully requested. The Examiner is invited to contact Applicant's below-named attorney, Philip F. Fox, as appropriate to facilitate allowance of the above-identified application.

Respectfully submitted,

KINNEY & LANGE, P.A.

Date: March 19, 2004

By _____

Philip F. Fox, Reg. No. 38,142
THE KINNEY & LANGE BUILDING
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Fax: (612) 339-6580

PFF:UNC:hlw

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

EXHIBIT A

of

AMENDMENT

U.S. PATENT NO. 6,297,027
ISSUED TO SPURLOCK

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
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Docket No.	:	LL31.12-0015	

EXHIBIT A

of

DECLARATION
UNDER
37 C.F.R. 1.131

LETTER OF BRIAN HOFFMAN OF NATIONAL BIOSCIENCES, INC. TO DR. JI

Exhibit A

NBI

Software and Research Services for Tomorrow's Discoveries

National Biosciences, Inc.
3650 Annapolis Lane North, #140
Plymouth, MN 55447-5434

Fax: 612.550.9625
Telephone: 612.550.2012

, 199

Dr.Shaoquan Ji
Purina Research Farm
100 Danforth Drive
Gary Summit, MO 63039

Dear Dr.Ji:

Please find enclosed your sequence from the 450 base clone.

If you have any questions or concerns, please call.

Sincerely,

Brian Hoffman

Brian Hoffman
National Biosciences, Inc.

Inquiries, Orders and Technical Support

Telephone: 800.747.4362
Fax: 800.369.5118
E-Mail: nbi@biotechnet.com

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
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EXHIBIT B

of

AMENDMENT

THE LANGUAGE OF BIOTECHNOLOGY, A DICTIONARY OF TERMS, PAGE 13 (SECOND EDITION, AMERICAN CHEMICAL SOCIETY, 1995) HIGHLIGHTING THE TERM "ALLELE"

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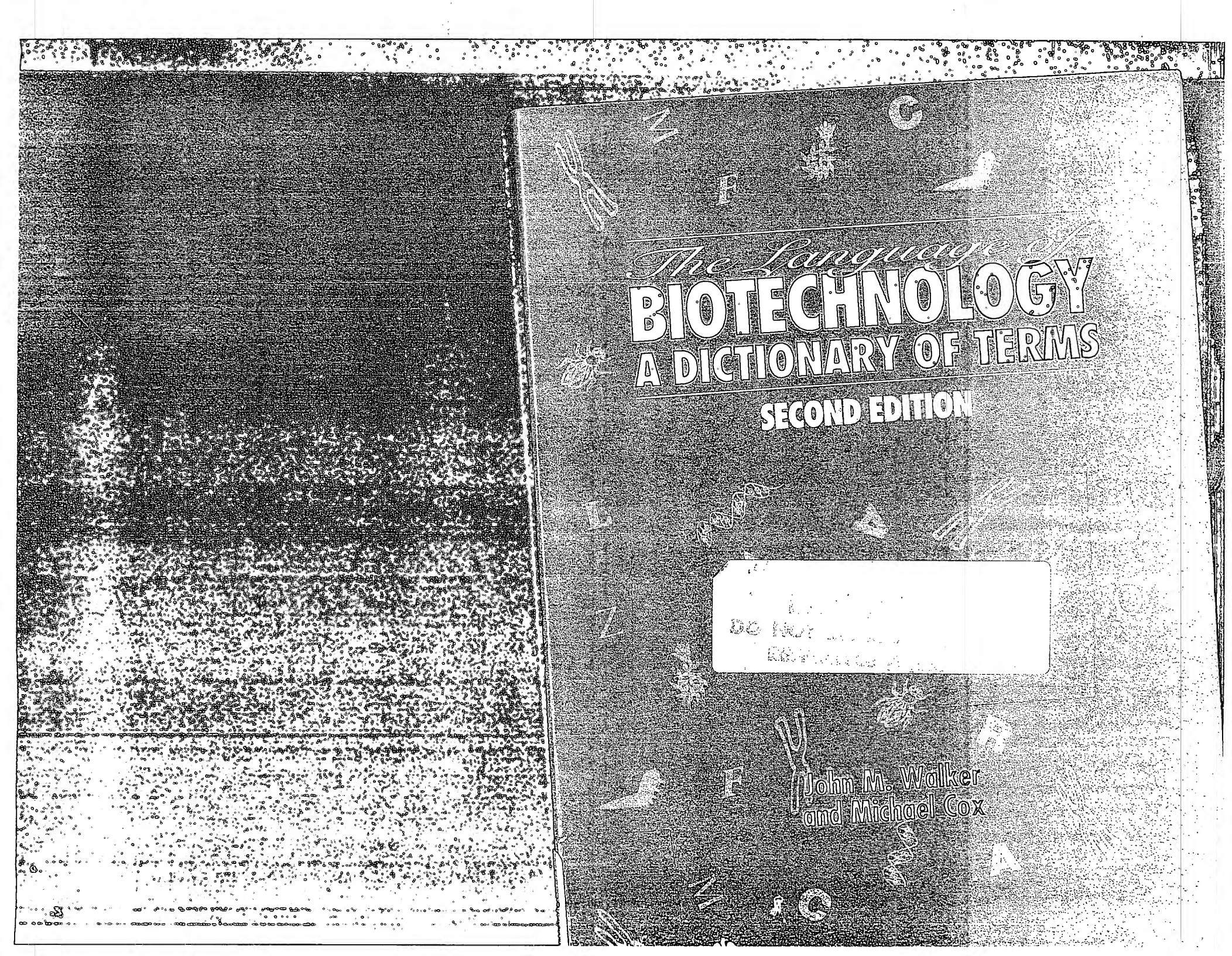
The Language of
BIOTECHNOLOGY
A DICTIONARY OF TERMS
SECOND EDITION
John M. Walker
and Michael Cox

Library of Congress Cataloging-in-Publication Data

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ISBN (invalid) 084122957

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I. Cox, Michael, 1933–. II. Whitaker, Allan. III. American Chemical Society. IV. Title.

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PRINTED IN THE UNITED STATES OF AMERICA

The Language of BIOTECHNOLOGY
A DICTIONARY OF TERMS
SECOND EDITION

John M. Walker
University of Hertfordshire

Michael Cox
University of Hertfordshire

Allan Whitaker, Contributor
University of Hertfordshire

Stephen Hall, Contributor
University of Hertfordshire

ACS Professional Reference Book

American Chemical Society, Washington, DC 1995

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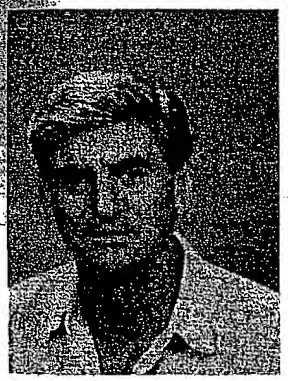
PRINTED IN THE UNITED STATES OF AMERICA

About the Authors

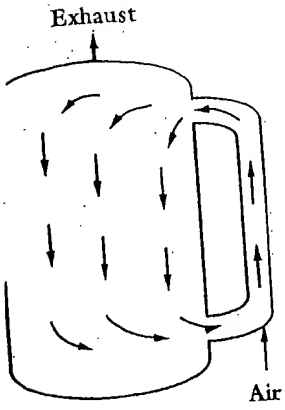


JOHN M. WALKER joined the Division of Biosciences at the University of Hertfordshire (formerly Hatfield Polytechnic) in 1980 and is currently their Head of Biochemistry and Director of the Science Training Center in the School of Natural Sciences. He was awarded a readership in protein chemistry in 1986 and was awarded the title of Professor in 1991.

Before that he was a postdoctoral research scientist at the Institute of Cancer Research, London, for eight years. Walker received a First Class Honors degree in chemistry and a Ph.D. in biological chemistry from University College, London.

For many years he was involved in studies on nonhistone chromosomal proteins. At the University of Hertfordshire he has been increasingly interested in algal biotechnology, particularly the use of algae as a source of novel pharmaceutical compounds, and in the studies of the factors responsible for protein stability.

Since 1981 he has been the organizer of the highly successful Techniques in Protein Chemistry laboratory workshops. These workshops are held annually at Hatfield and have also been run in Yugoslavia, Malaysia, Indonesia, Spain, Turkey, Egypt, Italy, Pakistan, and India. He has served as editor of a wide range of books on molecular biology methodology and is currently editor-in-chief of the journal *Molecular Biotechnology*.



(c) With external loop

:gories of seed storage proteins. *See*

. centrifugal device for liquid–liquid
bowl rotating about a central shaft.
:h spirally wound baffles to control
les also provide regions of intense
bowl periphery and the lighter fluid
now obsolete. *See also* Podbielniak

ılticellular eukaryotic aquatic plants.
. classification systems also include the
-green algae, although ideally they are
ı freshwater and marine environments
on of a range of compounds including
:y are also used as a source of pigment
ovide single-cell protein, particularly
ina is produced in Israel and Mexic
food in Japan). The fouling of wat
ustrial processes, swimming pools, a

algal oxidation pond \'al-gəl ˌäk-sə-'dā-shən 'pänd\ A large, shallow lagoon used for wastewater treatment. Wastewater is treated by the combined action of bacteria and photosynthetic algae. The algae produce oxygen and therefore maintain aerobic conditions. *See also* oxidation pond.

algicides \'al-jə-ˌsīdz\ Chemical agents that selectively kill algae.

alginate \'al-jə-ˌnāt\ A polysaccharide comprising D-mannuronic and L-guluronic acids. Traditionally it has been produced from marine algae (e.g., *Laminaria* species and *Macrocystis pyrifera*), but the source is subject to considerable variation. Alginate is also produced commercially from *Azobacter vinelandii*, but this microbial source differs from the algal source in having *O*-acetyl groups associated with D-mannuronic acid residues. Alginates are used as thickening and gelling agents in dairy products and in textile printing, and alginate gels have been used to immobilize cells and microorganisms by entrapment methods.

alkaline phosphatase (E.C. 3.1.3.1) \'al-kə-līn 'fäs-fə-ˌtās\ An enzyme (esterase) usually isolated from *Escherichia coli* or calf intestinal tissue, which hydrolyzes phosphate esters and has an optimum pH in the range 9–11. It is used to remove phosphate groups from 5′ termini of linear DNA molecules (e.g., a restricted plasmid molecule). This removal prevents recircularization of the restricted plasmid molecule by ligase during gene cloning experiments, thus ensuring that the intact circular molecules generated by the ligase contain an inserted gene. The enzyme is also commonly used in enzyme–antibody conjugates in techniques such as ELISA and immunohistochemistry.

alkaline proteases \'al-kə-līn 'prōt-ē-ˌās-əz\ Proteases with an optimum pH in the range 8–11. Industrially important alkaline proteases are produced from *Bacillus* species, especially *Bacillus licheniformis*, which produces the enzyme *subtilisin Carlsberg* (E.C. 3.4.21.14), one of the major constituents of enzyme detergents. Alkaline proteases are used in washing powders and for dehairing hides.

alkaloids \'al-kə-ˌlȯidz\ Naturally occurring organic compounds that possess marked pharmacological activity (not necessarily beneficial) in humans. Alkaloids are generally heterocyclic compounds of complex structure. Many alkaloids are found in plants, and a number have found use as drugs (e.g., atropine, colchicine, morphine, quinine, and scopolamine). Other alkaloids include cocaine, caffeine, nicotine, opium, and strychnine.

allele \ə-'lē(ə)l\ Any of one or more alternative forms of a given gene. They occur by mutation, where deletions, substitutions, or insertions have altered the original specific sequence of nucleotides. In a diploid cell or organism, the two alleles of a given gene occur in corresponding positions (loci) on a pair of homologous chromosomes. If these alleles are genetically identical, the cell or organism is said to be *homozygous*. If they are genetically different, it is *heterozygous* with respect to that gene.

allogenic \ˌal-ō-jə-'nē-ik\ Genetically dissimilar.

allograft (allogenic graft) \'al-əˌgraft (ˌal-ō-jə-'nē-ik 'graft)\ A graft between genetically dissimilar individuals of the same species.

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

EXHIBIT B

of

DECLARATION
UNDER
37 C.F.R. 1.131

SEQUENCE LISTING OF 450 BASE CLONE THAT ACCOMPANIED THE LETTER OF EXHIBIT A OF BRIAN HOFFMAN OF NATIONAL BIOSCIENCES, INC. TO DR. JI

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          10         20         30         40         50         60
AGCGCTGCAT TCAGGGCTGA GGTCCAGCTG CCGCAACATG TCCTGTAGTG ACCCCTGCAG
TCGCGACGTA AGTCCCGACT CCAGGTCGAC GGCGTTGTAC AGGACATCAC TGGGGACGTC

          70         80         90        100        110        120
CCGGCTCAGG GCCACCACCT CGGTGGAGTA GAGGGAGGCT TCCAGGACGA CACCCAAGCT
GGCCGAGTCC CGGTGGTGGA GCCACCTCAT CTCCCTCCGA AGGTCCTGCT GTGGGTTCGA

         130        140        150        160        170        180
CTCCAAGCTC TCCAGGGCCC TGAACTGCGG CAAGGGGCAG CTCTTGGAGG CGGCCAGCAG
GAGGTTCGAG AGGTCCCGGG ACTTGACGCC GTTCCCCGTC GAGAACCTCC GCCGGTCGTC

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CACCTCTTCC AGGGCCTCCA AGAGGTCCAG TAACCTATAA ACCTGGTGTA AAGACCTTCC

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GTCTGACCAC TCCTAGACAA CCATCTAGCG GTTACAGACC AGGTAGAACC TGTTTGAGTC

         310        320        330        340        350        360
GAGAGGGTGG AGCCCAGGGA TGAAGTCCAA ACCAGTGACC CTCTGTTTGG AGGAGACGGA
CTCTCCCACC TCGGGTCCCT ACTTCAGGTT TGGTCACTGG GAGACAAACC TCCTCTGCCT

         370        380        390        400        410        420
CTGCGTGTGT GAGATGTCAT TGATCCTGGT GACAATTGTC TTGATGAGGG TTTTGGTGTC
GACGCACACA CTCTACAGTA ACTAGGACCA CTGTTAACAG AACTACTCCC AAAACCACAG

         430        440        450        460        470        480
ATCCTGGACT TTTTGGATAG GCACGGCCT. .......... .......... ..........
TAGGACCTGA AAAACCTATC CGTGCCGGA. .......... .......... ..........
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First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

EXHIBIT C

of

AMENDMENT

DICTIONARY OF MICROBIOLOGY AND MOLECULAR BIOLOGY, PAGE 819
(3RD EDITION, JOHN WILEY & SONS, LTD, 2001)
HIGHLIGHTING THE TERM "VARIANT"

Dictionary of Microbiology and Molecular Biology

3rd Edition

Paul **Singleton**
Diana **Sainsbury**

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Paperback edition 1993
Reprinted 1993, 1994, 1995, 1996 (twice), 1997 (twice), 1999, 2000

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ISBN 0-471-94150-6 (cased) – ISBN 0-471-49064-4 (pbk.)
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Typeset in 10/12pt Times by Laser Words Pvt. Ltd., Chennai, India
Printed and bound in Great Britain by Antony Rowe Ltd, Chippenham, Wiltshire
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the virus) may be infected and may allow expression of viral early genes. Thus, e.g., a recombinant vaccinia virus containing a cDNA encoding Sindbis virus structural proteins has been used to infect cultured mosquito cells; infected cells were not lysed, and Sindbis virus proteins were synthesized and processed in their cytoplasm [JGV (1985) *66* 2761–2765]. Recombinant vaccinia viruses which can express antigens from unrelated pathogens (e.g. hepatitis B virus surface antigen [Nature (1983) *302* 490–495], or the circumsporozoite protein of a malarial parasite [Parasitol. (1986) *92* S109–S117]) have been suggested as 'live' vaccines against diseases caused by those pathogens [commentary: Nature (1986) *319* 549–550]. (See also AIDS.)

Vacuolaria See CHLOROMONADS.

vacuolating agent SIMIAN VIRUS 40.

vacuole Any of various membrane-delimited compartments within a cell: see e.g. CONTRACTILE VACUOLE, FOOD VACUOLE, GAS VACUOLE. In yeasts such as *Saccharomyces cerevisiae*, vacuoles function e.g. as repositories for the storage of e.g. POLYPHOSPHATE and certain amino acids, and apparently also function as LYSOSOMES, sequestering e.g. proteases and other hydrolytic enzymes. In mycelial fungi, vacuoles occupy a large proportion of the interior of older parts of the mycelium, possibly serving e.g. to concentrate the bulk of the cytoplasm at the growing hyphal tip (see GROWTH (b)).

vacuum autoclave See AUTOCLAVE.

vacuumizing See CANNING.

vagina microflora In adult women (post-puberty, pre-menopause) the vagina harbours a varied microflora in which species of *Lactobacillus* (particularly *L. acidophilus*) typically predominate; these bacteria metabolize glycogen and/or its breakdown products (present in the vaginal secretions), thus maintaining a low pH (< ca. 4.5) in the vagina – which helps to protect against CANDIDIASIS, TRICHOMONIASIS, and other vaginal infections (see also BACTERIAL VAGINOSIS). Other organisms which may be present in the vagina in a high proportion of healthy women include e.g. species of *Acinetobacter*, *Bacteroides*, *Bifidobacterium*, *Corynebacterium*, members of the Enterobacteriaceae, *Moraxella*, *Peptococcus*, *Peptostreptococcus*, *Staphylococcus*, *Streptococcus*, *Ureaplasma*, etc. [Changes in the vagina microflora during the menstrual cycle: AJRIM (1985) *9* 1–5.] Before puberty and after the menopause, the vagina is less acidic and it harbours a microflora which may include e.g. corynebacteria, enterobacteria, streptococci, etc. (See also GENITOURINARY TRACT FLORA.)

Vaginicola See PERITRICHIA.

vaginitis Inflammation of the vagina; it may involve any of a range of organisms: see e.g. CANDIDIASIS, TRICHOMONIASIS. (cf. BACTERIAL VAGINOSIS.) In *vulvovaginitis* both the vulva and vagina are affected. (See also ZEARALENONE.)

vaginosis See BACTERIAL VAGINOSIS.

Vahlkampfia A genus of amoebae (order SCHIZOPYRENIDA) in which flagellate stages are unknown. Cysts are commonly formed. Species are mainly free-living in freshwater, soil and marine habitats; *V. patuxent* is parasitic in the alimentary tract in oysters. (See also BEE DISEASES.)

VAHS (virus-associated haemophagocytic syndrome) See HAEMOPHAGOCYTIC SYNDROME.

valaciclovir An ANTIVIRAL AGENT used in the treatment of alphaherpesvirus infections; valaciclovir is the L-valyl ester of ACYCLOVIR.

valency (*immunol.*) The number of COMBINING SITES per monomeric or polymeric ANTIBODY; the term is sometimes also used to refer to the number of DETERMINANTS per antigen. (See also POLYVALENT ANTISERUM; POLYVALENT VACCINE.)

valid publication See NOMENCLATURE.

L-valine biosynthesis See Appendix IV(b).

valinomycin A DEPSIPEPTIDE ANTIBIOTIC, produced by *Streptomyces* sp, which can act as a mobile carrier IONOPHORE for the UNIPORT of Rb^+, K^+, Cs^+, or NH_4^+ across mitochondrial, thylakoid, bacterial or artificial membranes; valinomycin has a ca. 10^4-fold lower selectivity for Na^+ than for K^+. Valinomycin is a cyclic molecule containing 12 residues: (–D-valine–L-lactic acid–L-valine–D-α-hydroxyisovaleric acid–)$_3$; a single ion can be carried at the centre of the molecule – any ion being carried having, of necessity, previously lost its water of hydration. Valinomycin can be used e.g. to alter or abolish a membrane potential (see CHEMIOSMOSIS).

valley fever *Syn.* COCCIDIOIDOMYCOSIS.

Valonia A genus of marine, mainly tropical, siphonocladous green algae (division CHLOROPHYTA) in which the cells are inflated to form macroscopic vesicles.

VAMP See TETANOSPASMIN.

Vampirovibrio A genus of Gram-negative bacteria which are predatory on viable cells of *Chlorella*; a predatory bacterium attaches to the prey cell and grows without penetration (cf. BDELLOVIBRIO). The organisms are vibrioid, 0.3–0.6 μm in diameter, and each cell has a single, polar, non-sheathed flagellum. GC%: ca. 50. Type species: *V. chlorellavorus*.

Vampyrella See FILOSEA.

***van* genes** (*vanA, vanB*) See ENTEROCOCCUS.

vancomycin A complex glycopeptide ANTIBIOTIC produced by certain actinomycetes. Vancomycin inhibits PEPTIDOGLYCAN biosynthesis by binding to the D-alanyl-D-alanine of the pentapeptide in the bactoprenol-bound disaccharide–pentapeptide – thus preventing transfer of the disaccharide–pentapeptide from the membrane to the periplasmic site of incorporation.

Vancomycin is active against many Gram-positive bacteria; it is used clinically e.g. in the treatment of pseudomembranous colitis and infections involving MRSA. (Most Gram-negative bacteria are resistant as they are impermeable to the drug.)

Structurally related antibiotics (also obtained from actinomycetes) with apparently similar modes of action include actaplanin, actinoidin, AVOPARCIN, RISTOCETIN and TEICOPLANIN.

[Enterococci resistant to vancomycin: Drugs (1996) *51* (supplement 1) 6–12. Screening for vancomycin-resistant enterococci with multiplex PCR: JCM (1999) *37* 2090–2092. Reduced susceptibility of MRSA to vancomycin: JAC (1997) *40* 135–136; Lancet (1999) *353* 1587–1588.]

vanillin 3-Methoxy-4-hydroxybenzaldehyde.

Vannella See AMOEBIDA and PSEUDOPODIUM.

vapam *Syn.* METHAM SODIUM.

var. VARIETY (q.v.).

variable region (V region) (*immunol.*) Any of the four regions of a given type of (monomeric) Ig molecule (see IMMUNOGLOBULINS) in which compositional variation is most marked among antibodies of different specificity; one V region occurs (as a DOMAIN) at the N-terminal end of each heavy chain and light chain. (See also COMBINING SITE; HYPERVARIABLE REGION.)

variant A strain which differs from other related strains in a (specified or unspecified) way. (cf. VARIETY.)

variant antigen type See VSG.

variant surface glycoprotein See VSG.

varicella *Syn.* CHICKENPOX.

varicella-zoster virus See ALPHAHERPESVIRINAE.

variegation (*plant pathol.*) Patchy – or otherwise irregular – colour variation in leaves, petals etc; variegation may be genetically based or may result from e.g. virus infection. (cf. COLOUR-BREAKING; MOSAIC; MOTTLE.)

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

EXHIBIT C

of

DECLARATION
UNDER
37 C.F.R. 1.131

DATABASE PRINTOUT OF THE GENE SEQUENCE (IN SINGLE STRAND FORM) OF THE 450 BASE CLONE

Exhibit C

: SMTP%""WojciechRychlik"<nbi@epx.cis.umn.edu>" -199 . :40.85
JSHAOQUAN

: SEQUENCE

Dr. JI,

following is the sequence for your 450 base clone.
.ll be sending your project dut today for delivery on Monday.

:EQUENCE OF 450 BASE CLONE

REVERSE PRIMER SENT->

```
    10         20         30         40         50         60
:CTGCAT TCAGGGCTGA GGTCCAGCTG CCGCAACATG TCCTGTAGTG ACCCCTGCAG

    70         80         90        100        110        120
:CTCAGG GCCACCACCT CGGTGGAGTA GAGGGAGGCT TCCAGGACGA CACCCAAGCT

   130        140        150        160        170        180
:AAGCTC TCCAGGGCCC TGAACTGCGG CAAGGGGCAG CTCTTGGAGG CGGCCAGCAG

   190        200        210        220        230        240
:AGAAGG TCCCGGAGGT TCTCCAGGTC ATTGGATATT TGGACCACAT TTCTGGAAGG

   250        260        270        280        290        300
\CTGGTG AGGATCTGTT GGTAGATCGC CAATGTCTGG TCCATCTTGG ACAAACTCAG

   310        320        330        340        350        360
\GGGTGG AGCCCAGGGA TGAAGTCCAA ACCAGTGACC CTCTGTTTGG AGGAGACGGA

   370        380        390        400        410        420
:GTGTGT GAGATGTCAT TGATCCTGGT GACAATTGTC TTGATGAGGG TTTTGGTGTC

   430        440        450        460        470        480
:TGGACT TTTTGGATAG GCACGGCCT. ..........  ..........  ..........
```

<- FORWARD PRIMER SENT

RFC 822 Headers

```
eived: by decvax (UCX V2.0)
     Fri,              14:23:35 -0500
eived: from dialup-1-70.gw.umn.edu by epx.cis.umn.edu id SMTP-00130631be0019455; Fri,
m: "Wojciech Rychlik" <nbi@epx.cis.umn.edu>
ly-To: "Wojciech Rychlik" <nbi@epx.cis.umn.edu>
 JSHAOQUAN@DECVAx.PURINA-MILLS.COM
ject: SEQUENCE
e: Fri,           15:26:15 -0500
```

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

EXHIBIT D

of

AMENDMENT

DECLARATION UNDER 37 C.F.R §1.131 FROM PARENT APPLICATION NO. 08/688,908

Practiti ner's Dock t No. PM-8808 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Spurlock, Michael E.

Serial No.: 08/ 688,908 Group No.: 1804
Filed: July 31, 1996 Examiner: Nelson, Amy J.
For: Bovine Leptin Protein, Nucleic Acid Sequences Coding Therefor and Uses Thereof

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF PRIOR INVENTION IN THE UNITED STATES OR IN A NAFTA OR WTO MEMBER COUNTRY TO OVERCOME CITED PATENT OR PUBLICATION (37 C.F.R. 1.131)

PURPOSE OF DECLARATION

1. This declaration is to establish completion of the invention in this application in the United States, at a date prior to December 27, 1995, that is the effective date of the prior art:

   ☒ publication
   ☐ patent

that was cited by the

   ☒ examiner.
   ☐ applicant.

CERTIFICATE OF MAILING/TRANSMISSION (37 C.F.R. 1.8(a))

I hereby certify that this correspondence is, on the date shown below, being:

MAILING

☑ deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: October 1, 1997

FACSIMILE

☐ transmitted by facsimile to the Patent and Trademark Office.

Jere L. Houk

Signature

Jere L. Houk

(type or print name of person certifying)

From these documents and/or models, it can be seen that the invention in this application was made

- ☐ on _____.
- ☒ at least by the date of December 26, 1995, which is a date earlier than the effective date of the reference.

NOTE: *"If the dates of the exhibits have been removed or blocked off, the matter of dates can be taken care of in the body of the oath or declaration." M.P.E.P. § 715.07.*

NOTE: *"The dates in the oath or declaration may be the actual dates, or, if the applicant or patent owner does not desire to disclose his or her actual dates he or she may merely allege that the acts referred to occurred prior to a specified date." M.P.E.P. § 715.07.*

DILIGENCE

NOTE: *"Where there has not been reduction to practice prior to the date of the reference, the applicant or patent owner must also show diligence in the completion of his or her invention from a time just prior to the date of the reference continuously up to the date of the actual reduction to practice or up to the date of filing his or her application (filing constitutes a* ***constructive*** *reduction to practice, § 1.131)." M.P.E.P. § 715.07 (emphasis added).*

NOTE: *"A conception of an invention, though evidenced by disclosure, drawings, and even a model, is not a complete invention under the patent laws, and confers no rights on an inventor, and has no effect on a subsequently granted patent to another, UNLESS HE OR SHE FOLLOWS IT WITH REASONABLE DILIGENCE BY SOME OTHER ACT, such as an actual reduction to practice or filing an application for a patent. Automatic Weighing Mach. Co. v. Pneumatic Scale Corp., Limited 1909 C.D. 498, 139 O.G. 991.*

"Conception in the mental part of the inventive act, but it must be capable of proof, as by drawings, complete disclosure to another person, etc. In Mergenthaler v. Scudder, 1897 C.D. 724, 81 O.G. 1417, it was established that conception is more than a mere vague idea of how to solve a problem; the means themselves and their interaction must be comprehended also." M.P.E.P. § 715.07.

NOTE: *Only diligence before reduction to practice is a material consideration. The "lapse of time between the completion or reduction to practice of an invention and the filing of an application thereon" (Ex parte Merz 74 USPQ 296) is not relevant to an affidavit or declaration under 37 C.F.R. 1.131. M.P.E.P. § 715.07(a).*

Attached is a statement establishing the diligence of the applicants, from the time of their conception, to a time just prior to the date of the reference, up to the:

- ☐ actual reduction to practice.
- ☐ filing of this application.

TIME OF PRESENTATION OF THE DECLARATION

(complete (a), (b) or (c))

(a) ☐ This declaration is submitted prior to final rejection.

(b) ☒ This declaration is submitted with the first response after final rejection, and is for the purpose of overcoming a new ground of rejection or requirement made in the final rejection.

(c) ☐ This declaration is submitted after final rejection. A showing under 37 C.F.R. 1.116(b) is submitted herewith.

NOTE: *"When any claim of an application or a patent under reexamination is rejected under 35 U.S.C. 102(a) or (e), or 35 U.S.C. 103 based on a U.S. patent to another or others which is prior art under 35 U.S.C. 102(a) or (e) and which substantially shows or describes but does not claim the same patentable invention, as defined in 37 C.F.R. 1.601(n), or on reference to a foreign patent or to a printed publication, the inventor of the subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§ 1.42, 1.43 or 1.47, may submit an appropriate oath or declaration to overcome the patent or publication. The oath or declaration must include facts showing a completion of the invention in this country or in a NAFTA or WTO member country before the filing date of the application on which the U.S. patent issued, or before the date of the foreign patent, or before the date of the printed publication. When an appropriate oath or declaration is made, the patent or publication cited shall not bar the grant of a patent to the inventor or the confirmation of the patentability of the claims of the patent, unless the date of such patent or printed publication is more than one year prior to the date on which the inventor's or patent owner's application was filed in this country." 37 C.F.R. § 1.131(a)(1).*

NOTE: *37 C.F.R. 1.131 is not applicable to a rejection based on a U.S. patent that CLAIMS the rejected invention.*

2. The person making this declaration is (are):

☒ the inventor(s).

☐ only some of the joint inventor(s)
(and a suitable excuse is attached for failure of the omitted joint inventor(s) to sign)

☐ the party in interest
(and a suitable explanation as why it is not possible to produce the declaration of the inventor(s) is attached)

FACTS AND DOCUMENTARY EVIDENCE

3.

NOTE: *"The showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application." 37 C.F.R. § 1.131(b).*

To establish the date of completion of the invention of this application, the following attached documents and/or models are submitted as evidence:

(check all applicable items below)

☒ Sequence Alignments

☐ blueprints

☐ photographs

☐ reproduction(s) of notebook entries

☐ model

☐ supporting statement(s) by witness(es) (where verbal disclosures are the evidence relied upon)

NOTE: *While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See Mergenthaler v. Scudder 1897 C.D. 724, 81 O.G. 1417." M.P.E.P. § 715.*

DECLARATION

6. As a person signing below:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE(S)

7. *(complete A or B below)*

A. Inventor(s)

Full name of **sole** or **first** inventor Michael E. Spurlock

Inventor's signature Michael E. Spurlock

Date 9/29/97 Country of Citizenship USA

Residence Pacific, Missouri

Post Office Address 410 Henry's Trace

Pacific, Missouri 63069

Full name of **second** joint inventor, if any _____

Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

(use added page for signature by additional inventors)

Number of pages added: 0

SCORES Initl: 1365 Initn: 1365 Opt: 1395
87.6% identity in 445 bp overlap

```
                                    449       439       429       420
Bobji.                                AGGCCGTGCCTATCCAAAAAGTCCAGGATG
                                      | || ||||| ||||||||||||||| ||||
Hsul89 TGTGGCTTTGGCCCTATCTTTTCTATGTCCAAGCTGTGCCCATCCAAAAAGTCCAAGATG
       30        40        50        60        70        80

     419       409       399       389       379       369       360
Bobji. ACACCAAAACCCTCATCAAGACAATTGTCACCAGGATCAATGACATCTCACACACGCAGT
       ||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Hsul89 ACACCAAAACCCTCATCAAGACAATTGTCACCAGGATCAATGACATTTCACACACGCAGT
       90        100       110       120       130       140

     359       349       339       329       319       309       300
Bobji. CCGTCTCCTCCAAACAGAGGGTCACTGGTTTGGACTTCATCCCTGGGCTCCACCCTCTCC
       | ||||||||||||||||  ||||| |||||||||||||| |||||||||||||  |||
Hsul89 CAGTCTCCTCCAAACAGAAAGTCACCGGTTTGGACTTCATTCCTGGGCTCCACCCCATCC
       150       160       170       180       190       200

     299       289       279       269       259       249       240
Bobji. TGAGTTTGTCCAAGATGGACCAGACATTGGCGATCTACCAACAGATCCTCACCAGTCTGC
       |||  || ||||||||||||||||||| ||||  |||||||||||||||||||||| |||
Hsul89 TGACCTTATCCAAGATGGACCAGACACTGGCAGTCTACCAACAGATCCTCACCAGTATGC
       210       220       230       240       250       260

     239       229       219       209       199       189       180
Bobji. CTTCCAGAAATGTGGTCCAAATATCCAATGACCTGGAGAACCTCCGGGACCTTCTCCACC
       |||||||||| ||| |||||||||||| |||||||||||||||||||| ||||| |||
Hsul89 CTTCCAGAAACGTGATCCAAATATCCAACGACCTGGAGAACCTCCGGGATCTTCTTCACG
       270       280       290       300       310       320

     179       169       159       149       139       129       120
Bobji. TGCTGGCCGCCTCCAAGAGCTGCCCCTTGCCGCAGTTCAGGGCCCTGGAGAGCTTGGAGA
       ||||||||  ||| |||||||||| ||||||   | ||| | |||||||| |||||| |
Hsul89 TGCTGGCCTTCTCTAAGAGCTGCCACTTGCCCTGGGCCAGTGGCCTGGAGACCTTGGACA
       330       340       350       360       370       380

     119       109       99        89        79        69        60
Bobji. GCTTGGGTGTCGTCCTGGAAGCCTCCCTCTACTCCACCGAGGTGGTGGCCCTGAGCCGGC
       || |||| |  |||||||||| ||   ||||||||| |||||||||||||||||| |||
Hsul89 GCCTGGGGGGTGTCCTGGAAGCTTCAGGCTACTCCACAGAGGTGGTGGCCCTGAGCAGGC
       390       400       410       420       430       440

     59        49        39        29        19        9
obji. TGCAGGGGTCACTACAGGACATGTTGCGGCAGCTGGACCTCAGCCCTGAATGCAGCGCT
       |||||||||| || ||||||||| || |||||||||||||||||||  ||| |
sul89 TGCAGGGGTCTCTGCAGGACATGCTGTGGCAGCTGGACCTCAGCCCTGGGTGCTGA
     450       460       470       480       490       500


obji.Seq /rev
bn:Humob

OCUS       HUMOB          644 bp    mRNA            PRI
EFINITION  Human mRNA for ob.
CCESSION   D49487
```

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

EXHIBIT E

of

AMENDMENT

U.S. PATENT APPLICATION PUBLICATION NO. US 2003/0219819 A1
ENTITLED "METHOD FOR IMPROVING
EFFICIENCIES IN LIVESTOCK PRODUCTION",
INVENTED BY MARQUESS, FOLEY LEIGH SHAW,
(REFERRED TO AS THE "FOLEY PUBLICATION")

US 20030219819A1

(19) United States

(12) Patent Application Publication (10) Pub. No.: US 2003/0219819 A1

Marquess (43) Pub. Date: Nov. 27, 2003

(54) METHOD FOR IMPROVING EFFICIENCIES IN LIVESTOCK PRODUCTION

(76) Inventor: Foley Leigh Shaw Marquess, Alberta (CA)

Correspondence Address:
JUDY JARECKI-BLACK; PH.D., J.D.
3239 SATELLITE BLVD. 3RD FLOOR
DULUTH, GA 30096 (US)

(21) Appl. No.: 10/442,662

(22) Filed: May 21, 2003

(30) Foreign Application Priority Data

May 21, 2002 (CA) 2,387,003

Publication Classification

(51) Int. Cl.[7] C12Q 1/68; A01K 67/027; A01K 31/19

(52) U.S. Cl. 435/6; 800/14; 119/300

(57) ABSTRACT

A method for improving efficiencies in livestock production comprises grouping livestock animals, such as cattle and pigs, during the period of their retention in a feeding facility according to the genetic predisposition of individual livestock animals to deposit fat, and then feeding the animals in each group substantially uniformly. Such genetic predisposition is determined by determining homozygosity or heterozygosity of each animal with respect to alleles of a gene encoding an adipocyte-specific polypeptide, termed leptin, which gene is hereinafter referred to as ob, segregating such animals into groups based on genotype and optionally phenotype, feeding and otherwise maintaining animals in a group together and apart from other groups of animals, and ceasing to feed the animals in the group at a time when the median body fat condition of the animals of that group is a desired body fat condition. Packers can also more accurately predict the fat deposition in carcasses of live animals it purchases, leading to increased efficiencies.

Exhibit E

KEYWORDS .
SOURCE Homo sapiane fat cDNA to mRNA.
ORGANISM Homo sapiens . . .

SCORES Initl: 1062 Initn: 1332 Opt: 1364
86.8% identity in 447 bp overlap

```
                                    449       439       429       420
Bobji.                                AGGCCGTGCCTATCCAAAAAGTCCAGGATG
                                      | || ||||| |||||||||||||| ||||
Jumob  TGTGGCTTTGGCCCTATCTTTTCTATGTCCAAGCTGTGCCCATCCAAAAAGTCCAAGATG
         50        60        70        80        90       100

     419       409       399       389       379       369       360
Bobji. ACACCAAAACCCTCATCAAGACAATTGTCACCAGGATCAATGACATCTCACACACGCAGT
       |||||||||||||||||||||||||||||||||||||||||||||||| ||||||||   ||
Jumob  ACACCAAAACCCTCATCAAGACAATTGTCACCAGGATCAATGACATTTCACACAC---GT
         110       120       130       140       150       160

     359       349       339       329       319       309       300
Bobji. CCGTCTCCTCCAAACAGAGGGTCACTGGTTTGGACTTCATCCCTGGGCTCCACCCTCTCC
       | ||||||||||||||| ||||| |||||||||||||| |||||||||||||   |||
Jumob  CAGTCTCCTCCAAACAGAAAGTCACCGGTTTGGACTTCATTCCTGGGGTCCACCCCATCC
           170       180       190       200       210       220

     299       289       279       269       259       249       240
Bobji. TGAGTTTGTCCAAGATGGACCAGACATTGGCGATCTACCAACAGATCCTCACCAGTCTGC
       |||  || ||||||||||||||||| |||| |||||||||||||||||||||| |||
Jumob  TGACCTTATCCAAGATGGACCAGACACTGGCAGTCTACCAACAGATCCTCACCAGTATGC
           230       240       250       260       270       280

     239       229       219       209       199       189       180
Bobji. CTTCCAGAAATGTGGTCCAAATATCCAATGACCTGGAGAACCTCCGGGACCTTCTCCACC
       |||||||||| ||| |||||||||||| |||||||||||||||||| ||||| |||
Jumob  CTTCCAGAAACGTGATCCAAATATCCAACGACCTGGAGAACCTCCGGGATCTTCTTCACG
           290       300       310       320       330       340

     179       169       159       149       139       129       120
Bobji. TGCTGGCCGCCTCCAAGAGCTGCCCCTTGCCGCAGTTCAGGGCCCTGGAGAGCTTGGAGA
       |||||||| ||| |||||||||| ||||||  | ||| | |||||||| |||||| |
Jumob  TGCTGGCCTTCTCTAAGAGCTGCCACTTGCCCTGGGCCAGTGGCCTGGAGACCTTGGACA
           350       360       370       380       390       400

     119       109        99        89        79        69        60
Bobji. GCTTGGGTGTCGTCCTGGAAGCCTCCCTCTACTCCACCGAGGTGGTGGCCCTGAGCCGGC
       || |||| |  |||||||||| ||   ||||||||| |||||||||||||||||| |||
Jumob  GCCTGGGGGGTGTCCTGGAAGCTTCAGGCTACTCCACAGAGGTGGTGGCCCTGAGCAGGC
           410       420       430       440       450       460

      59        49        39        29        19         9
Bobji. TGCAGGGGTCACTACAGGACATGTTGCGGCAGCTGGACCTCAGCCCTGAATGCAGCGCT
       |||||||||| || ||||||||| || |||||||||||||||||||  ||| | |
Jumob  TGCAGGGGTCTCTGCAGGACATGCTGTGGCAGCTGGACCTCAGCCCTGGGTGCTGAGGCC
           470       480       490       500       510       520

Jumob  TTGAAGGTCACTCTTCCTGCAAGACTACGTTAAGGGAAGGAACCTGGCTTCAGGTATCTC
           530       540       550       560       570       580
```

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

EXHIBIT F

of

AMENDMENT

DECLARATION UNDER 37 C.F.R §1.131 IN PRESENT APPLICATION NO. 09/928,522

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor	:	Michael E. Spurlock	
Appln. No.	:	09/928,522	
Filed	:	August 13, 2001	Group Art Unit: 1647
Title	:	Bovine Leptin Protein, Antisense and Antibody	Examiner: C. J. Saoud
Docket No.	:	LL31.12-0015	

DECLARATION UNDER 37 C.F.R. § 1.131

MS Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

SENT VIA EXPRESS MAIL

Express Mail No.: EV 302264737 US

Sir:

This Declaration is to establish completion of the invention in the above-identified patent application in the United States at a date prior to December 27, 1995, which is the effective date of the prior art publication TELLAM et al. (Genbank Acc. No. U43943, Bos taurus OBESE mRNA, 27 January 1996), hereinafter referred to as the "Tellam submission." The Examiner cited the Tellam Submission in the Office Action mailed in the above-identified application on September 22, 2003. To establish the date of completion of the invention of this application, evidence that the invention was completed (reduced to practice) on or before December 26, 1995, which is a date earlier than the effective date (December 27, 1995) of the Tellam submission, is provided. Since the invention was reduced to practice prior to the effective date of the Tellam submission, there is no requirement to establish due diligence with regard to reduction to practice of the invention.

I, Michael E. Spurlock declare:

1. I am the sole inventor of the invention of the above-identified application, as defined in claims 1-5 of the above-identified patent application.

2. Claim 1 of the above-identified application presently reads as follows:

> ***1. An isolated single or double-stranded DNA molecule which encodes a bovine adipocyte polypeptide leptin, the molecule consisting of the nucleotide sequence SEQ ID NO:3 or an allelic variant thereof.***

3. Claim 5 of the above-identified application presently reads as follows:

> ***5. (Original) An isolated mRNA molecule for encoding a bovine adipocyte polypeptide leptin, the mRNA molecule encoded by the nucleotide sequence of SEQ ID NO:3 or an allelic variant thereof.***

4. On or before December 26, 1995, I completed (reduced to practice) the invention of the above-identified application, as defined in claims 1 and 5 of the above-identified patent application, as evidenced by the following:

A. Copies of various documents are attached as Exhibits A-C of this Declaration. Each of the documents of Exhibits A-C were created on or before December 26, 1995. Various dates have been redacted from one or more of the documents of Exhibits A-C. Each of the dates redacted from any of the documents of Exhibits A-C is on or before December 26, 1995.

B. During the period ending on or before December 26, 1995 when I completed (reduced to practice) the invention of the above-identified application, as defined in claims 1 and 5 of the above-identified patent application, I was employed as a research scientist by Purina Mills, Inc.

C. During the period ending on or before December 26, 1995 when I completed (reduced to practice) the invention of the above-identified application, Dr. Shaoquan Ji, a post-doctorate researcher, worked under my direction in my laboratory at Purina Mills, Inc.

D. During the period ending on or before December 26, 1995 when I completed (reduced to practice) the invention of the above-identified application, Dr. Ji, pursuant to my instructions and under my direction, isolated a 450 base clone that constituted the nucleotide sequence of SEQ ID NO:3 or an allelic variant thereof, that is presently defined in both claims 1 and 5 of the above-identified application, as explained more fully below:

i. First, Dr. Ji, pursuant to my instructions and under my direction, extracted total RNA from bovine adipose tissue that encoded for a bovine adipocyte polypeptide.

ii. The total RNA extraction referenced in §4.D.i. above was accomplished using an acidic guanidinium thiocyanate-phenol-chloroform extraction technique based on the method of Chomczynski and Saachi (Chomczynski and Sacchi, 1987, Analytic Biochemistry 162:156).

iii. After extracting the total RNA, Dr. Ji, pursuant to my instructions and under my direction, purified the total RNA and reverse transcribed the purified total RNA into a single-stranded bovine leptin cDNA product using a reverse transcriptase from Gibco BRL of Gaithersburg, MD.

iv. Then, Dr. Ji, pursuant to my instructions and under my direction, amplified the single-stranded bovine leptin cDNA product referenced in §4.D.iii. above to a double-stranded bovine leptin cDNA product via a Polymerase Chain Reaction (PCR) using synthetic DNA primers based on the published mouse leptin cDNA sequence.

v. The synthetic DNA primers referenced in §4.D.iv. above were designed to amplify the coding region of the bovine leptin gene while excluding the secretory signal at the 5'-terminal of the coding region.

vi. After amplifying the single-stranded bovine leptin cDNA product to a double-stranded bovine leptin cDNA product as described in §4.D.iv. above, Dr. Ji, pursuant to my instructions and under my direction, purified the double-stranded bovine leptin cDNA product and thereafter isolated the 450 base clone that constituted the nucleotide sequence of SEQ ID NO:3 or an allelic variant thereof presently defined in both claims 1 and 5 of the above-identified application.

E. During the period ending on or before December 26, 1995 when I completed (reduced to practice) the invention of the above-identified application, Dr. Ji, pursuant to my instructions and under my direction, sent the 450 base clone

referenced in ¶4.D.vi. above to National Biosciences, Inc. (a commercial laboratory skilled in gene sequencing and gene sequencing protocol) with instructions to sequence the 450 base clone referenced in ¶4.D.vi. above.

F. In response to the instructions referenced in ¶4.E. above, Brian Hoffman of National Biosciences, Inc. sent Dr. Ji a letter (attached as Exhibit A of this Declaration) with an enclosed paper (attached as Exhibit B of this Declaration) that listed the sequence of the 450 base clone referenced in ¶4.D.vi. above.

G. Under my direction, the gene sequence of the 450 base clone referenced in ¶4.D.vi. above, was converted from the double-stranded form (see Exhibit B of the Declaration) into a single-stranded gene sequence form that was entered into a database for further software-driven analysis; a printout of the gene sequence (in single strand form) of the 450 base clone from the database is attached as Exhibit C of this Declaration.

H. The facts and evidence presented in ¶¶ 4. D(i.-vi.) and 4.E.-4.G above demonstrate that, during the period ending on or before December 26, 1995, I completed (reduced to practice) the invention of the above-identified application, as defined in claim 1, which defines: "An isolated single or double-stranded DNA molecule which encodes a bovine adipocyte polypeptide leptin, the molecule consisting of the nucleotide sequence SEQ ID NO:3 or an allelic variant thereof." The 450 base clone discussed in ¶4.D.vi. above is the "isolated single or double-stranded DNA molecule defined in claim 1.

I. The facts and evidence presented in ¶¶ 4. D(i.-vi.) and 4.E.-4.G above demonstrate that, during the period ending on or before December 26, 1995, I completed (reduced to practice) the invention of the above-identified application, as defined in claim 5, which defines: "An isolated mRNA molecule for encoding a bovine adipocyte polypeptide leptin, the mRNA molecule encoded by the nucleotide sequence of SEQ ID NO:3 or an allelic variant thereof." The purified total RNA defined mentioned in ¶¶4.D.iii. includes the isolated mRNA molecule defined in claim 5.

J. The 450 base clone discussed in ¶4.D.vi. above could not have been produced from bovine adipose tissue via the acidic guanidinium thiocyanate-phenol-chloroform extraction technique procedure mentioned in ¶4.D.ii. without first producing the purified total RNA defined mentioned in ¶¶4.D.iii. above.

K. The facts and evidence presented in ¶¶ 4. D(i.-vi.) and 4.E.-4.J above demonstrate that, during the period ending on or before December 26, 1995, I completed (reduced to practice) the invention, as defined in claims 1 and 5, of the above-identified application.

5. All of the acts referenced above, or documented by Exhibits A-C, occurred in the United States.

6. This Declaration is being submitted prior to issuance of any final Office Action in the above-identified application and is therefore timely-filed.

I declare that all statements made herein that are of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that the

statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

INVENTOR:

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Citizenship: U.S.A.

Date: March 18, 2004

Michael E. Spurlock
Signature

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obji.Seq /rev
b_Ro:Mmu18812

OCUS       MMU18812     2793 bp    mRNA            ROD
EFINITION  Mus musculus obese precursor (ob) mRNA, complete cds.
CCESSION   U18812
EYWORDS    .
OURCE      mouse.
 ORGANISM  Mus musculus . . .


CORES           Initl:  1297 Initn:  1297 Opt:  1304
          84.7% identity in 445 bp overlap

                                    449       439       429       420
obji.                                 AGGCCGTGCCTATCCAAAAAGTCCAGGATG
                                      | || |||||||||||| ||||||||||||
Mmul88 TGTGGCTTTGGTCCTATCTGTCTTATGTTCAAGCAGTGCCTATCCAGAAAGTCCAGGATG
          90        100       110       120       130       140

    419       409       399       389       379       369       360
Bobji. ACACCAAAACCCTCATCAAGACAATTGTCACCAGGATCAATGACATCTCACACACGCAGT
       |||||||||||||||||||||| |||||||||||||||||||||||| ||||||||||||
Mmul88 ACACCAAAACCCTCATCAAGACCATTGTCACCAGGATCAATGACATTTCACACACGCAGT
          150       160       170       180       190       200

    359       349       339       329       319       309       300
Bobji. CCGTCTCCTCCAAACAGAGGGTCACTGGTTTGGACTTCATCCCTGGGCTCCACCCTCTCC
       | || ||| |||| |||||||||||||| |||||||||| |||||||| |||||  | |
Mmul88 CGGTATCCGCCAAGCAGAGGGTCACTGGCTTGGACTTCATTCCTGGGCTTCACCCCATTC
          210       220       230       240       250       260

    299       289       279       269       259       249       240
Bobji. TGAGTTTGTCCAAGATGGACCAGACATTGGCGATCTACCAACAGATCCTCACCAGTCTGC
       |||||||||||||||||||||||||| ||||  |||| |||||| |||||||||| ||||
Mmul88 TGAGTTTGTCCAAGATGGACCAGACTCTGGCAGTCTATCAACAGGTCCTCACCAGCCTGC
          270       280       290       300       310       320

    239       229       219       209       199       189       180
Bobji. CTTCCAGAAATGTGGTCCAAATATCCAATGACCTGGAGAACCTCCGGGGACCTTCTCCACC
       |||||  ||||||| | || ||| ||||||||||||||| ||||| ||||| ||||| |
Mmul88 CTTCCCAAAATGTGCTGCAGATAGCCAATGACCTGGAGAATCTCCGAGACCTCCTCCATC
          330       340       350       360       370       380

    179       169       159       149       139       129       120
Bobji. TGCTGGCCGCCTCCAAGAGCTGCCCCTTGCCGCAGTTCAGGGCCCTGGAGAGCTTGGAGA
       ||||||||  |||||||||||||| || |||| |||  ||| | |||| |||     ||||
Mmul88 TGCTGGCCTTCTCCAAGAGCTGCTCCCTGCCTCAGACCAGTGGCCTGCAGAAGCCAGAGA
          390       400       410       420       430       440

    119       109        99        89        79        69        60
Bobji. GCTTGGGTGTCGTCCTGGAAGCCTCCCTCTACTCCACCGAGGTGGTGGCCCTGAGCCGGC
       || ||| || |||||||||||||| |||||||||| |||||||||| |||||  |||
Mmul88 GCCTGGATGGCGTCCTGGAAGCCTCACTCTACTCCACAGAGGTGGTGGCTTTGAGCAGGC
          450       460       470       480       490       500

      59        49        39        29        19         9
Bobji. TGCAGGGGTCACTACAGGACATGTTGCGGCAGCTGGACCTCAGCCCTGAATGCAGCGCT
       ||||||| || || ||||||||  | |  ||| ||||  | ||||||||||| |
Mmul88 TGCAGGGCTCTCTGCAGGACATTCTTCAACAGTTGGATGTTAGCCCTGAATGCTGAAGTT
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        510       520       530       540       550       560
mu188 TCAAAGGCCACCAGGCTCCCAAGAATCATGTAGAGGGAAGAAACCTTGGCTTCCAGGGGT
        570       580       590       600       610       620


obji.Seq /rev
b_Ro:Mmu22421

OCUS       MMU22421     2235 bp    DNA             ROD
EFINITION  Mus musculus obesity protein (ob) gene, complete cds.
CCESSION   U22421
EYWORDS    .
OURCE      mouse.
 ORGANISM  Mus musculus . . .


CORES            Initl:   950 Initn:  1237 Opt:   995
          82.5% identity in 359 bp overlap

       389       379       369       359       349       339
obji. GTCACCAGGATCAATGACATCTCACACACGCAGTCCGTCTCCTCCAAACAGAGGGTCACT
                                    ||||| || ||| |||| ||||||||||||
mu224 ACACCTCTTGTTCTTCTTCCTCCTCCATATCAGTCGGTATCCGCCAAGCAGAGGGTCACT
      1850      1860      1870      1880      1890      1900

       329       319       309       299       289       279
obji. GGTTTGGACTTCATCCCTGGGCTCCACCCTCTCCTGAGTTTGTCCAAGATGGACCAGACA
      || ||||||||||| |||||||| |||||  | ||||||||||||||||||||||||||
mu224 GGCTTGGACTTCATTCCTGGGCTTCACCCCATTCTGAGTTTGTCCAAGATGGACCAGACT
      1910      1920      1930      1940      1950      1960

       269       259       249       239       229       219
obji. TTGGCGATCTACCAACAGATCCTCACCAGTCTGCCTTCCAGAAATGTGGTCCAAATATCC
      ||||  |||| ||||||  |||||||||| |||||||||  |||||||  | || ||| ||
mu224 CTGGCAGTCTATCAACAGGTCCTCACCAGCCTGCCTTCCCAAAATGTGCTGCAGATAGCC
      1970      1980      1990      2000      2010      2020

       209       199       189       179       169       159
obji. AATGACCTGGAGAACCTCCGGGACCTTCTCCACCTGCTGGCCGCCTCCAAGAGCTGCCCC
      |||||||||||||| ||||| ||||| ||||| |||||||||  |||||||||||| ||
mu224 AATGACCTGGAGAATCTCCGAGACCTCCTCCATCTGCTGGCCTTCTCCAAGAGCTGCTCC
      2030      2040      2050      2060      2070      2080

       149       139       129       119       109        99
obji. TTGCCGCAGTTCAGGGCCCTGGAGAGCTTGGAGAGCTTGGGTGTCGTCCTGGAAGCCTCC
      ||||  |||  |||  | ||||  |||     |||||| ||| || ||||||||||||||
mu224 CTGCCTCAGACCAGTGGCCTGCAGAAGCCAGAGAGCCTGGATGGCGTCCTGGAAGCCTCA
      2090      2100      2110      2120      2130      2140

        89        79        69        59        49        39
obji. CTCTACTCCACCGAGGTGGTGGCCCTGAGCCGGCTGCAGGGGTCACTACAGGACATGTTG
      |||||||||||  ||||||||||  ||||| |||||||||| || || ||||||||  |
mu224 CTCTACTCCACAGAGGTGGTGGCTTTGAGCAGGCTGCAGGGCTCTCTGCAGGACATTCTT
      2150      2160      2170      2180      2190      2200

        29        19         9
obji. CGGCAGCTGGACCTCAGCCCTGAATGCAGCGCT
      |  ||| ||||  | ||||||||||| |
mu224 CAACAGTTGGATGTTAGCCCTGAATGCTGA
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